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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,927	06/24/2003	Jean Merrill	USAV2001/0172USNP	1793
5487	7590	07/13/2007		
ROSS J. OEHLER SANOFI-AVENTIS U.S. LLC 1041 ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			EXAMINER XIE, XIAOZHEN	
			ART UNIT 1646	PAPER NUMBER
			NOTIFICATION DATE 07/13/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/602,927	Applicant(s) MERRILL ET AL.	
	Examiner Xiaozhen Xie	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,6 and 7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,6 and 7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>20070614</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

The Information Disclosure Statement (IDS) filed 14 June 2007 has been entered. Applicant's amendment of the claims received on 26 April 2007 is acknowledged.

Claims 2, 4, 5 and 8-17 are cancelled. Claims 1, 3, 6 and 7 are pending and under examination in this office action.

Claim Rejections Maintained

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The amended claims 1, 3, 6 and 7 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement for reasons set forth in the previous office actions.

Applicant argues that claims 1 and 3 have been amended to recite that oligodendrocytes are "primary oligodendrocytes", and that the cell lines that Selvaraju used are not primary oligodendrocytes and have different characteristics than primary oligodendrocytes. Applicant argues that the Louis reference shows that CG4 cells can express GFAP and become astrocytes, which would never happen to normal oligodendrocyte progenitors. Applicant cites Cao et al. showing the advantages of using oligodendrocyte precursor cells isolated from the developing rat optic nerve. Applicant

Art Unit: 1646

argues that the experiments on differentiation of primary oligodendrocytes are different from that of cell lines, and the conclusion from the experiments (models/assays) of the instant invention is not surprisingly different from that of Selvaraju.

Applicants' argument has been fully considered but has not been found to be persuasive.

As stated in the previous office action (15 November 2006), Selvaraju used two oligodendrocyte precursors (OLPs) cell lines: Oli-neu and CG-4 for the *in vitro* studies, and both cell lines have been well-characterized and further demonstrated in the Selvaraju study for being suitable for myelination (i.e., oligodendrocyte differentiation) studies in the nervous system. Louis developed the CG-4 cell line, and characterized the cells as "undistinguishable from primary O-2A cells by morphological and immunochemical criteria" (pp. 194, left column, last paragraph in Introduction), and O-2A cells are oligodendrocyte-type 2-astrocyte progenitors isolated from the optic nerve from the newborn rat (pp. 194, right column, section "O-2A Cell Culture"). It is not true that normal oligodendrocyte progenitors can never differentiate into astrocytes. Crang et al. (Eur. J. Neurosci., 2004, 20(6):1445-1460) teach that myelin oligodendrocyte glycoprotein (MOG)-expressing oligodendrocyte precursors isolated from the adult rat CNS (primary culture) can differentiate into oligodendrocytes, or astrocytes and Schwann cells, depending on the culture medium components (see Abstract). The results of Selvaraju's study using two different OLP cell lines are consistent that recombinant OPN induces proliferation of oligodendrocyte precursor cells and stimulates differentiation. Further, Selvaraju used mixed cortical cultures from

Art Unit: 1646

embryonic mouse brain (an *in vitro* primary culture model of myelination), and showed that recombinant OPN stimulated both myelin basic protein (MBP, the mature oligodendrocyte marker) synthesis and myelin sheath formation (pp. 715, left column, section *Recombinant OPN enhances myelin formation in vitro*). This data supports the involvement of OPN in the development of oligodendrocytes. Applicant asserts that the experiments on differentiation of primary oligodendrocytes are different from that of cell lines, and that the conclusion from the experiments (models/assays) of the instant invention is not surprisingly different from that of Selvaraju. However, Applicant has not provided any examples or evidence showing such difference. Since Selvaraju teaches a method of inducing differentiation of oligodendrocyte precursor cells and enhancing remyelination by increasing exposure of oligodendrocyte precursor cells to OPN, which is in contradiction to the method of the instant invention, and the specification, has failed to provide any objective evidence or working examples, one skilled in the art would not know how to practice the claimed invention without undue experimentation.

In addition, claims 1 and 3 recite "reducing exposure of oligodendrocytes and precursors thereof to osteopontin". However, the specification fails to teach how to achieve such "reducing exposure", for example, in an *in vivo* system. The specification teaches using an antibody that specifically binds to OPN, or by inactivating OPN receptor with an OPN antagonist or an antibody. The specification, however, fails to teach such antibody or how to inactivate the OPN receptor using said agents. There is no teaching in the specification as to how to make and use these agents. Clearly, it

Art Unit: 1646

would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the invention as now claimed: "primary oligodendrocytes". The instant specification as filed does not provide sufficient written description for the limitation. Applicant's amendment, filed 26 April 2007, asserts that no new matter has been added. However, the instant specification as filed does not provide sufficient written description for the limitation of "primary oligodendrocytes". This is a new matter rejection.

Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites "The method of claim 10", and claim 10 has been cancelled.

Claim 6 depends from claim 7.

Conclusion

NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1646

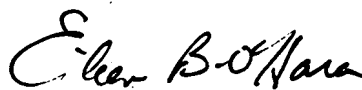
the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
June 29, 2007


EILEEN B. O'HARA
PRIMARY EXAMINER